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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/826,797	04/16/2004	Robert B. Fick	P0957R1C1	1468

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EXAMINER	
SZPERKA, MICHAEL EDWARD	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/826,797	FICK ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19,40 and 44-65* is/are pending in the application.

4a) Of the above claim(s) *6,8,44-48 and 50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-5, 7, 9-19, 40, 49, and 51-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response and amendments received July 26, 2006 are acknowledged.

Claims 1, 11, 12, 19, 40, 44-50 have been amended.

Claims 51-65 have been added.

Claims 1-19, 40, and 44-65 are pending in the instant application.

Claims 6, 8, 44-48 and 50 stand withdrawn from consideration as being drawn to nonelected species. See 37 CFR 1.142(b) and MPEP § 821.03, for reasons of record set forth in the restriction requirements mailed 3.22/05 and 9/7/05.

Claims 1-5, 7, 9-19, 40, 49, and 51-65 are under examination in the instant office action as they read on a method of treating late asthmatic response (LAR) by administering a humanized anti-IgE antibody.

Applicant's amendment to the first line of the specification to update priority information is acknowledged.

The declaration of Yamo Deniz, M.D. under 37 CFR 1.132 is acknowledged. The declaration will be discussed below in conjunction with applicant's arguments concerning the claim rejections.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. The rejection of claims 40 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite has been withdrawn in light of applicant's claim amendments received 7/26/06.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. The rejection of claims 40 and 49 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement has been withdrawn in light of applicant's claim amendments received 7/26/06 which delete the term "adjuvant" form the claimed invention.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. The rejection of claim 40 under 35 U.S.C. 102(b) as being anticipated by Jardieu et al. (WO 93/04173, of record) has been withdrawn in view of applicant's claim amendments received 7/26/06.

Specifically, the claim amendments received 7/26/03 have remove antihistamines from the group of additional secondary agents that are to be administered in conjunction with anti-IgE antibodies. Jardieu et al. teach that therapeutic methods of administering anti-IgE antibodies are to be combined with other well known therapies, but they do not specifically teach the instant recited agents.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1, 5, 7, 9-12, 16, and 18 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Jardieu et al. (WO 93/04173, of record as document 35 on the IDS received 7/30/04, see entire document) in view of Larsen et al (of record as document 227 on the IDS received 7/30/04, see entire document).

The office action mailed 1/26/06 states:

> Jardieu et al. teach methods of administering humanized anti-IgE antibodies for therapy and prophylaxis of allergic and other IgE-mediated disorders (see entire document, particularly the abstract and lines 30-34 of page 6). Note that a prophylactic dose would necessarily be given prior to the onset of symptoms, while a therapeutic dose would be given subsequent to the development of symptoms. One particular anti-IgE antibody taught by Jardieu et al. is humanized e25, the same antibody used in the working examples of the instant application, which is taught as binding soluble IgE but not IgE bound to FcεRI present on cells such as basophils (see particularly lines 7-17 of page 7). It is also disclosed that these antibodies are to be administered with other known anti-allergic compounds including antihistamines (see particularly lines 19-24 of page 43). Anti-IgE antibodies are taught as being administered at concentrations that are greatly in excess of serum IgE such that the antibodies effectively prevent binding of endogenous IgE to its receptors (see particularly the paragraph that spans pages 42 and 43). These teachings differ from the instant claimed method in that while they teach methods for the therapy and prophylaxis of allergic and other IgE-mediated disorders and teach that IgE mediates asthma (see particularly lines 8-11 of page 1), these teachings do not specify that the late asthmatic response (LAR) is an IgE mediated disorder.
>
> Larsen et al. teach that LAR is an IgE mediated disorder because LAR is dependent upon the presence of antigen-specific IgE (see entire document, particularly the last sentence of the upper paragraph of page 253).
>
> Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to administer anti-IgE antibodies to treat LAR. Motivation to do so comes from the teachings of Larsen et al. that LAR is an IgE-mediated condition that is dependent upon the presence of antigen-specific IgE and the teachings of Jardieu et al. that anti-IgE antibodies are to be administered for treatment and prophylaxis of IgE-mediated disorders. Note that while these teachings do indicate that administering anti-IgE antibodies reduces free IgE concentration (see particularly lines 30-38 of page 1 of Jardieu et al.), they do not teach the specific value of less than 40 ng/mL. However, it is inherent that administration of anti-IgE antibodies would result in such a decrease, especially given that the humanized antibody disclosed by Jardieu et al. and the humanized antibody used in the working examples of the instant invention is the same antibody.

Applicant's arguments filed 7/26/06 have been fully considered but they are not persuasive. Applicant first argues that Jardieu et al. does not teach a therapeutic

method wherein a baseline IgE level is obtained before administering an anti-IgE antibody.

This argument is not convincing because Jardieu et al. teach that determining the administered dosage of an IgE antagonist is routine in the art and depends upon many factors known to the clinician (see from line 17 of page 42 to line 24 of page 43). One specific factor discussed is the administration of a dosage that can effectively compete with endogenous IgE, and as such Jardieu et al. teach methods wherein patient IgE levels are measured since one cannot administer a competitive dose if the endogenous level of IgE is unknown (see particularly from line 32 of page 42 to line 5 of page 43).

Applicant also argues that it does not logically follow that the methods taught by Jardieu et al. result in a reduction of IgE to 40 ng/ml since Jardieu et al. do not teach how much anti-IgE therapeutic should be administered to achieve a reduction of free to a given fixed level (i.e. 40 ng/ml). This argument is not convincing because neither the independent claim nor dependent claim 16 which recites reducing a patients serum IgE to about 40 ng/ml recite a specific dose of IgE antagonist that is to be administered. As such, applicant is arguing limitations not claimed.

Applicant further argues that at the time of the invention, a skilled artisan would not believe the teachings of Larsen et al. that the late asthmatic response is an IgE-mediated disorder based upon their work in a rabbit model system. To support this argument, applicant has provided the declaration of Yamo Deniz, M.D. under 37 CFR 1.132. In this declaration, Yamo Deniz states his opinion that a skilled artisan would not have believed the conclusions taught by Larsen et al. (i.e. that the late asthmatic response is an IgE-mediated disorder) because controls and additional experiments believed by Yamo Deniz to be necessary to support the conclusions of Larsen et al. are not present. Yamo Deniz also states "it is difficult, if not impossible to extrapolate meaningful conclusions regarding the pathology of human asthma from animal models of lower mammals such as rabbits and mice" based upon the teachings of Tepper et al. (abstract of record as document 304 on the 7/30/04 IDS) that neither mast cells nor IgE greatly influence anaphylaxis, airway hyperreactivity or airway inflammation in a murine asthma model.

These arguments and the declaration of Yamo Deniz are not convincing for the following reasons: First, Yamo Deniz is an employee of the assignee of the instant application. As such he is not a disinterested party in this application and his statements have been considered in this light.

Second, animal models, while often imperfect, are widely used and accepted in biomedical research since many experiments are either difficult or unethical to perform on humans. While the model of Tepper et al. indicates that IgE does not greatly influence anaphylaxis, airway hyperreactivity or airway inflammation in a murine asthma, it is not taught that IgE plays no role in asthma. Further, many other researcher using murine models have demonstrated a clear role for IgE in murine asthma (Coyle et al. (of record as reference 81 on the 7/30/04 IDS), Haile et al., and Mayr et al., see entire documents particularly the abstracts), and the model system of Larsen et al. involves rabbits, an organism not discussed by Tepper et al. Researchers would not use animal models if meaningful conclusions could not be extrapolated to human conditions, and given the art teachings concerning the involvement of IgE in asthma, including murine asthma, the statement of Yamo Deniz concerning animal models is not persuasive.

Yamo Deniz has also criticized the experimental design used by Larsen et al. in their 1984 paper. Subsequent work by Larsen et al. states "Therefore, like the skin, the lungs of both humans and rabbits can show antigen-induced physiological alterations in airway function associated with the presence of IgE hours after antigen exposure. Thus, this antibody isotype appears to be necessary to initiate a process that leads to the antigen-induced LAR." (Larsen et al., 1987, see entire document, particularly top of the left column of page 107). Additionally, Kay et al. teach in 1984 that "Thus, with allergen-inhalation challenge, there is strong evidence for believing that the initial immunological trigger, that is, antigen and mast cell-bound IgE, leads to the manifestations of both the early and late-phase responses." (of record as reference 191 on the 7/30/04 IDS, see particularly page 212). As such, the argument that a skilled artisan would not have believed the late asthmatic response to be mediated by IgE prior to the filing of the instant application does not appear to be in accord with the teachings

of the prior art. Also note that if the teachings of Larsen et al. and Kay et al. were incorrect (i.e. LAR is not mediated by IgE) applicant's instant invention would not work.

For all of these reasons applicant's arguments have not been found persuasive, and therefore the rejection is maintained.

10. Claims 2, 14, and 15 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Jardieu et al. (WO 93/04173, of record as document 35 on the IDS received 7/30/04, see entire document) in view of Larsen et al (of record as document 227 on the IDS received 7/30/04, see entire document) as applied to claims 1, 5, 7, 9-12, 16, and 18 above, and further in view of Rup et al. (US Patent No. 4,940,782, of record as document 4 on the IDS received 7/30/04, see entire document).
The office action mailed 1/26/06 states:

> The teachings of Jardieu et al. and Larsen et al. have been discussed above. These teachings differ from the instant invention in that they do not explicitly teach the repeated administration of anti-IgE antibodies in formulations comprising buffers and other additives.
>
> Rup et al. teach methods of administering anti-IgE antibodies. These antibodies are taught as being administered at dosages that can readily be determined by one of skill in the art, with such dosages being repeated daily or for a period of time (see particularly lines 50-65 of column 5). The anti-IgE antibodies are administered in formulations comprising buffers and preservatives (see entire document, particularly lines 3-18 of column 6. These formulations offer the advantage of allowing the anti-IgE antibodies to be administered by a variety of modes such as parenterally and intravenously.
>
> Therefore, a person of ordinary skill in the art at the time the invention was made would have been motivated to administer the anti-IgE antibodies taught by Jardieu et al. to treat LAR as taught by Jardieu et al. and Larsen et al. in formulations comprising buffers and other ingredients as taught by Rup et al. to gain the advantage of administering the anti-IgE antibodies by a variety of modes such as parenterally and intravenously. Note that freeze-drying of the anti-IgE antibody prior to its reconstitution in a pharmaceutical composition would not materially alter the structure or therapeutic properties of the antibody actually administered in such a composition, and as such dependent claim 15 has been included in this rejection. Note also that the claims do not require the loading and maintenance doses to differ in concentration.

Applicant's arguments filed 7/26/06 have been fully considered but they are not persuasive. Applicant argues that the deficiencies with the rejection under 103(a) of Jardieu et al. in view of Larsen et al. are not remedied by the addition of Rup et al.

This argument is not convincing for the reasons discussed above concerning the rejection based upon Jardieu et al. in view of Larsen et al.

The rejection is maintained.

11. Claims 3, 4, 13, 17, 19, and 51-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jardieu et al. (WO 93/04173, of record as document 35 on the IDS

received 7/30/04, see entire document) in view of Larsen et al (of record as document 227 on the IDS received 7/30/04, see entire document) and in view of Rup et al. (US Patent No. 4,940,782, of record as document 4 on the IDS received 7/30/04, see entire document) as applied to claims 1, 2, 5, 7, 9-12, 14-16, and 18 above, and further in view of Jardieu et al. (Jardieu2, US Patent No. 5,622,700, see entire document).

The office action mailed 1/26/06 states:

> The teachings of Jardieu et al., Larsen et al., and Rup et al. have been discussed above. These teachings differ from the instant invention in that they do not explicitly teach the administration of anti-IgE on a weekly or biweekly basis, or that an administered loading dose is greater than a maintenance dose.
>
> Jardieu2 teach that the administration of antibodies to treat chronic disorders, such as asthma, is to be done by administering the antibodies in an initial (i.e. loading) dose followed by maintenance dosing, wherein the maintenance doses are lower than the initial dose (see entire document, particularly lines 3-14 and 31-44 of column 7). The maintenance doses are taught as being administered either weekly or biweekly (see particularly from line 24 of column 12 to line 27 of column 13). Such as dosing regimen offers the advantage of providing the most efficacious therapeutic results (see particularly lines 1-12 of column 13).
>
> Therefore, a person of ordinary skill in the art at the time the invention was made would have been motivated to treat the IgE-mediated disease LAR as taught by Larson et al. by administering the humanized anti-IgE antibodies taught by Jardieu et al. in the formulations taught by Rup et al. using the dosage timings and amounts disclosed by Jardieu2 in order to gain the advantage of the most therapeutically efficacious manner of administering the anti-IgE antibody.

Applicant's arguments filed 7/26/06 have been fully considered but they are not persuasive. Applicant argues that the deficiencies with the rejection under 103(a) of Jardieu et al. in view of Larsen et al. and further in view of Rup et al. are not remedied by the addition of Jardieu2.

This argument is not convincing for the reasons discussed above concerning the rejections of record.

Applicant also argues that Jardieu2 teach dosing methodologies that use different antibodies in a different disease setting rather than anti-IgE in the treatment of asthma.

This argument is not convincing because it is routine for clinicians to optimize the timing, dosage and route of administration of agents in the treatment of a disease or condition. Further, Jardieu2 specifically teach that the use of high initial doses followed by lower maintenance doses provides a distinct advantage in therapeutic efficacy for antibodies of differing specificities for the treatment of multiple clinically and mechanistically distinct disorders, and as such it is reasonable to expect that such a

dosing regimen would provide similar benefits in the context of administering anti-IgE antibodies.

The rejection is maintained.

12. Claims 40 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jardieu et al. (WO 93/04173, of record as document 35 on the IDS received 7/30/04, see entire document) in view of Cockcroft et al. (J. Allergy Clin. Immunol. 1987, 79:734-740, of record as document 67 on the IDS received 7/30/04, see entire document).

The office action mailed 1/26/06 states:

> The teachings of Jardieu et al. have been discussed above. These teachings differ from the instant claimed invention in that while they teach the administration of anti-IgE antibodies to treat asthma, teach that anti-IgE antibodies are to be administered in combination with additional therapeutic agents commonly used for treatment of allergies, and give a non-limiting example of such an agent as being antihistamines, they do not teach administration with the elected species of steroids.
>
> Cockcroft et al. teach that administration of multiple anti-asthmatic agents offer an advantage because administration of only a single agent is often inadequate to clinically treat symptoms (see entire document, particularly the abstract and discussion section). It is further taught that steroids are desirable for combination therapy with anti-asthmatic agents since they have the advantageous property of being able to be administered prophylactically (see particularly the last sentence of the abstract and the last paragraph of the discussion on page 739).
>
> Therefore, a person of ordinary skill in the art at the time the invention was made would have been motivated to substitute steroids as taught by Cockcroft et al. for antihistamines in compositions comprising anti-IgE antibodies as taught by Jardieu et al. to gain the advantage of using an agent known to be effective in treating asthma that can be administered prophylactically.

Applicant's arguments filed 7/26/06 have been fully considered but they are not persuasive. First, applicant argues that while Jardieu et al. teach the combination of anti-IgE antibodies with other therapeutics such as histamines, they do not teach steroids, and that since Cockcroft et al. does not teach antihistamines in combination with his small molecule anti-asthmatic compounds, a skilled artisan would not have combined steroids and anti-IgE antibodies because they work by distinct biological pathways and that motivation to combine the agents does not come from the art but from applicant's disclosure.

This argument is not persuasive, because as discussed in the rejection of record, any single anti-asthmatic agent may be ineffectual when administered in isolation, and as such Cockcroft et al. advise administration of multiple agents to treat asthma, thus providing motivation in the art to combine agents. The agents taught by Cockcroft work

via distinct mechanistic pathways and therefore it is not reasonable that a skilled artisan would fail to co-administer a steroid with an anti-IgE antibody simply because they work via different pathways. Note also that antihistamines, like the bronchodilators and steroids taught by Cockcroft et al., are small molecules. Further, Jardieu et al. teach that asthma is an allergic disorder (lines 8-9 of page 1), that anti-IgE antibodies are to be combined with other known therapies for allergies (lines 19-21 of page 43), and disclose a non-exhaustive list of therapies that differ greatly in their mechanism of operation (lines 22-24 of page 43). Given that the teachings of Cockcroft et al. were published prior to Jardieu et al., they are clearly "known therapies" in the art for the treatment of the allergic disorder asthma.

Additionally, "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. . . [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205USPQ 1069, 1072 (CCPA 1980) (see MPEP 2144.06). Note that all the agents are taught in the art as being useful for treating allergic asthma.

Applicant's second argument is that neither reference either alone or in combination teaches measuring baseline IgE and then dosing relative to such levels to achieve therapeutic effect.

This argument is not convincing because the claims do not recite measuring baseline IgE or recite any therapeutic effect other than that allergic asthma is treated. Both references teach methods of treating allergic asthma, and as such the rejection is maintained.

13. Claims 40 and 49 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hardman et al. (EP 0 589 840 A1, of record as document 25 on the IDS received 7/30/04, see entire document) in view of Cockcroft et al. (J. Allergy Clin. Immunol. 1987,

79:734-740, of record as document 67 on the IDS received 7/30/04, see entire document).

The office action mailed 1/26/06 states:

> Hardman et al. teach methods of administering anti-IgE antibodies to treat allergic asthma (see entire document, particularly the abstract, lines 32-58 of page 15, and most particularly the sentence that spans pages 15 and 16). These teachings differ from the claimed invention in that they do not explicitly teach the administration of anti-IgE antibodies with additional active ingredients such as steroids.
>
> Cockcroft et al. teach that administration of multiple anti-asthmatic agents offer an advantage because administration of only a single agent is often inadequate to clinically treat symptoms (see entire document, particularly the abstract and discussion section). It is further taught that steroids are desirable for combination therapy with anti-asthmatic agents since they have the advantageous property of being able to be administered prophylactically (see particularly the last sentence of the abstract and the last paragraph of the discussion on page 739).
>
> Therefore, a person of ordinary skill in the art at the time the invention was made would have been motivated to treat allergic asthma by administering the anti-IgE antibodies of Hardman et al. in combination with steroids as taught by Cockcroft et al. to gain the advantage of increased therapeutic efficacy since administration of a single anti-asthmatic agent is often therapeutically inadequate as was taught by Cockcroft et al.

Applicant's arguments filed 7/26/06 have been fully considered but they are not persuasive. First, applicant argues that because the anti-IgE antibody of Hardman et al. is a protein based biological application and the molecules discussed by Cockcroft et al. are small molecules, a skilled artisan would not have been motivated to combine them into a single formulation for administration without reference to the instant application.

This argument is not persuasive, because as discussed in the rejection of record, any single anti-asthmatic agent may be ineffectual when administered in isolation, and as such Cockcroft et al. advise administration of multiple agents to treat asthma. The agents taught by Cockcroft work via distinct mechanistic pathways and therefore it is not reasonable that a skilled artisan would fail to co-administer an anti-IgE antibody simply because it works via a different pathway. Further, "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. . . [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205USPQ 1069, 1072 (CCPA 1980) (see MPEP 2144.06). Note that all the agents are taught in the art as being useful for treating allergic asthma.

Applicant's second argument is that neither reference either alone or in combination teaches measuring baseline IgE and then dosing relative to such levels to

achieve therapeutic effect.

This argument is not convincing because the claims do not recite measuring baseline IgE or recite any therapeutic effect other than that allergic asthma is treated. Both references teach methods of treating allergic asthma, and as such the rejection is maintained.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1, 5, 7, 9-10, and 12 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 9 of U.S. Patent No. 6,699,472 in view of Larsen et al. (of record as document 227 on the IDS received 7/30/04, see entire document).

The office action mailed 1/26/06 states:

> The claims of '472 recite a method of treating an allergic condition by administering a humanized anti-IgE antibody, and specifically recite the allergic condition asthma. The specification teaches that IgE mediates allergic disorders including asthma (see particularly lines 23-25 of column 1 and lines 38-52 of column 4), but it does not specify that LAR is an IgE-mediated allergic disorder. Note that the patented

claims are more narrowly drawn in that they recite anti-IgE antibodies rather than the more generic term IgE antagonists.

Larsen et al. teach that LAR is an IgE mediated disorder because LAR is dependent upon the presence of antigen-specific IgE (see entire document, particularly the last sentence of the upper paragraph of page 253).

Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to administer anti-IgE antibodies to treat LAR. Motivation to do so comes from the teachings of Larsen et al. that LAR is an IgE-mediated condition that is dependent upon the presence of antigen-specific IgE and the claims of '472 which teach treatment of allergic disorders by administering anti-IgE antibodies.

Applicant has acknowledged this rejection and requests that it be held in abeyance until the remaining rejections and objections are obviated.

Therefore, the rejection is maintained.

16. Claims 1, 5, 7, and 9-11 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 9 of U.S. Patent No. 6,685,939 in view of Larsen et al. (of record as document 227 on the IDS received 7/30/04, see entire document).

The office action mailed 1/26/06 states:

The claims of '939 recite a method inhibiting the onset of an allergic condition by administering a humanized anti-IgE antibody, and specifically recite the allergic condition asthma. The specification teaches that IgE mediates allergic disorders including asthma (see particularly lines 23-25 of column 1 and lines 38-52 of column 4), but it does not specify that LAR is an IgE-mediated allergic disorder. Note that the antibody must be administered prior to the onset of asthma symptoms in order to effectively inhibit the onset of asthma. Also note that the patented claims are more narrowly drawn in that they recite anti-IgE antibodies rather than the more generic term IgE antagonists.

Larsen et al. teach that LAR is an IgE mediated disorder because LAR is dependent upon the presence of antigen-specific IgE (see entire document, particularly the last sentence of the upper paragraph of page 253).

Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to administer anti-IgE antibodies to treat LAR. Motivation to do so comes from the teachings of Larsen et al. that LAR is an IgE-mediated condition that is dependent upon the presence of antigen-specific IgE and the claims of '939 which teach inhibiting the onset of asthma and other allergic disorders by administering anti-IgE antibodies.

Applicant has acknowledged this rejection and requests that it be held in abeyance until the remaining rejections and objections are obviated.

Therefore, the rejection is maintained.

17. Claims 40 and 49 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 9 of U.S. Patent No.

6,699,472 in view of Cockcroft et al. (J. Allergy Clin. Immunol. 1987, 79:734-740, of record as document 67 on the IDS received 7/30/04, see entire document).

The office action mailed 1/26/06 states:

> The claims of '472 recite a method of treating asthma by administering a humanized anti-IgE antibody. They differ from the instant claimed invention in that additional anti-asthmatic compounds are not recited as being concordantly administered, although they are narrower in scope since they recite anti-IgE antibodies rather than the more generic term IgE antagonists.
>
> Cockcroft et al. teach that administration of multiple anti-asthmatic agents offer an advantage because administration of only a single agent is often inadequate to clinically treat symptoms (see entire document, particularly the abstract and discussion section). It is further taught that steroids are desirable for combination therapy with anti-asthmatic agents since they have the advantageous property of being able to be administered prophylactically (see particularly the last sentence of the abstract and the last paragraph of the discussion on page 739).
>
> Therefore, a person of ordinary skill in the art at the time the invention was made would have been motivated to treat allergic asthma by administering the humanized anti-IgE antibodies recited in the methods of the '472 patent in combination with steroids as taught by Cockcroft et al. to gain the advantage of increased therapeutic efficacy since administration of a single anti-asthmatic agent is often therapeutically inadequate as was taught by Cockcroft et al.

Applicant has acknowledged this rejection and requests that it be held in abeyance until the remaining rejections and objections are obviated.

Therefore, the rejection is maintained.

18. Claims 40 and 49 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 5, and 6 of copending Application No. 11/013,966 in view of view of Cockcroft et al. (J. Allergy Clin. Immunol. 1987, 79:734-740, of record as document 67 on the IDS received 7/30/04, see entire document).

The office action mailed 1/26/06 states:

> The claims of application 11/013,966 teach a method of treating the IgE-mediated disorder allergic asthma by administering specific humanized anti-IgE antibodies. These claims differ from the instant claimed invention that that they do not recite that the anti-IgE antibodies are to be administered with an additional active ingredient such as a steroid, but are narrower in scope since they recite anti-IgE antibodies rather than the more generic term IgE antagonists.
>
> Cockcroft et al. teach that administration of multiple anti-asthmatic agents offer an advantage because administration of only a single agent is often inadequate to clinically treat symptoms (see entire document, particularly the abstract and discussion section). It is further taught that steroids are desirable for combination therapy with anti-asthmatic agents since they have the advantageous property of being able to be administered prophylactically (see particularly the last sentence of the abstract and the last paragraph of the discussion on page 739).
>
> Therefore, a person of ordinary skill in the art at the time the invention was made would have been motivated to treat allergic asthma by administering the humanized anti-IgE antibodies recited in the claims of copending application 11/013,966 in combination with steroids as taught by Cockcroft et al. to gain the advantage of increased therapeutic efficacy since administration of a single anti-asthmatic agent is often therapeutically inadequate as was taught by Cockcroft et al.

This is a provisional obviousness-type double patenting rejection.

Applicant has acknowledged this rejection and requests that it be held in abeyance until the remaining rejections and objections are obviated.

Therefore, the rejection is maintained.

19. Claims 1, 5, 7, 9, 10, 12, and 14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 3, 5, and 6 of copending Application No. 11/013,966 in view of view of Larsen et al. (of record as document 227 on the IDS received 7/30/04, see entire document).
The office action mailed 1/26/06 states:

> The claims of application 11/013,966 teach a method of treating IgE-mediated disorders by administering anti-IgE antibodies, including humanized antibodies, in formulations comprising buffers. A specifically recited humanized antibody, rhuMAbE25, is taught as binding free IgE but not binding FcεRI-bound IgE. These claims differ from the instant claimed invention that that they do not recite that the IgE-mediated disorder is LAR, but are more narrowly constructed than the instant claims in that they recite anti-IgE antibodies rather tan the more generic term IgE antagonists.
>
> Larsen et al. teach that LAR is an IgE mediated disorder because LAR is dependent upon the presence of antigen-specific IgE (see entire document, particularly the last sentence of the upper paragraph of page 253).
>
> Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to administer anti-IgE antibodies to treat LAR. Motivation to do so comes from the teachings of Larsen et al. that LAR is an IgE-mediated condition that is dependent upon the presence of antigen-specific IgE and the claims of copending application 11/013,966 which teach treatment of IgE-mediated disorders by administering anti-IgE antibodies.

This is a provisional obviousness-type double patenting rejection.

Applicant has acknowledged this rejection and requests that it be held in abeyance until the remaining rejections and objections are obviated.

Therefore, the rejection is maintained.

20. Claims 1, 5, 12, 14, and 15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 37, 44-46, and 49 of copending Application No. 09/705,457 in view of view of Larsen et al. (of record as document 227 on the IDS received 7/30/04, see entire document).
The office action mailed 1/26/06 states:

> The claims of application 09/705,457 recite a method of treating IgE-mediated disorders by administering anti-IgE antibodies, in formulations comprising buffers. The anti-IgE antibodies that are administered are recited as having been lyophilized prior to reconstitution for administration. These claims differ from the instant claimed invention that that they do not recite that the IgE-mediated disorder is LAR.

Note that the copending claims are more narrowly drawn in that they recite anti-IgE antibodies rather than the more generic term IgE antagonists.

Larsen et al. teach that LAR is an IgE mediated disorder because LAR is dependent upon the presence of antigen-specific IgE (see entire document, particularly the last sentence of the upper paragraph of page 253).

Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to administer anti-IgE antibodies to treat LAR. Motivation to do so comes from the teachings of Larsen et al. that LAR is an IgE-mediated condition that is dependent upon the presence of antigen-specific IgE and the claims of copending application 09/705,457 which teach treatment of IgE-mediated disorders by administering anti-IgE antibodies.

This is a provisional obviousness-type double patenting rejection.

Applicant has acknowledged this rejection and requests that it be held in abeyance until the remaining rejections and objections are obviated.

Therefore, the rejection is maintained.

Claim Objections

21. Claims 1 and 19 are objected to because they recite FceRI rather than FcεRI.

Claim 51 is objected to because the recitation of 10 mg/mg in line 2 of the claim appears to be a typographical error.

Claim 57 is objected to because if fails to further limit the claim from which it depends. Specifically, both recite a "maintenance dose of about 0.1 to about 10 mg/kg."

22. No claims are allowable.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Patent Examiner
Technology Center 1600
October 10, 2006

10/13/06

G.R. EWOLDT, PH.D.
PRIMARY EXAMINER